Open access • Journal Article • DOI:10.1002/MDS.23624

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Published on: 01 Jun 2011 - Movement Disorders (John Wiley & Sons, Ltd)

Topics: Dystonia, Deep brain stimulation and Essential tremor

Article

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SUPPLEMENT

Early Postoperative Management of DBS in Dystonia: Programming, Response to Stimulation, Adverse Events, Medication Changes, Evaluations, and Troubleshooting

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ABSTRACT: Early postoperative management in deep brain stimulation–treated patients with dystonia differs from that of patients with essential tremor and Parkinson's disease, mainly due to the usually delayed effects of deep brain stimulation and the heterogenous clinical manifestation and etiologies of dystonia. The present chapter summarizes the available data about and concentrates on practical clinical aspects of early postoperative management in deep brain stimulation–treated patients with dystonia. © 2011 *Movement* Disorder Society

Key Words: deep brain stimulation; dystonia; programming; parameter

Postoperative early management of patients with dystonia following deep brain stimulation (DBS) differs from that in patients with essential tremor (ET) or Parkinson's disease (PD) due to the usually delayed improvement of dystonic symptoms following initiation of DBS. In ET patients, rapid improvement of tremor is frequently observed within seconds, giving the neurosurgeon the immediate opportunity to optimize placement of the electrode position during the surgical procedure. Similarly, in PD patients, tremor and rigidity improve in seconds/minutes following the initiation of DBS, thus facilitating the selection of the therapeutically most efficacious electrode contacts, although treatment of levodopa-induced dyskinesias might require several adjustments of medications and DBS parameters. In addition, both ET and PD patients often benefit from a "lesion effect" in the immediate postoperative period, presumably because of the trauma induced by the insertion of the electrodes. Although this lesion-like effect has not been fully investigated and usually lasts from a few days to a few weeks, patients with dystonia seem to have less prominent clinical benefit from this effect. This observation might be related to the larger volume of the usual target in dystonia, the globus pallidus internus (GPi), compared with the smaller target volumes of the thalamic Vim in ET and the subthalamic nucleus in PD. Furthermore, DBS-induced effects in dystonia usually start to occur within several hours or days, with a very gradual progression of improvement that sometimes extends over prolonged periods of several months, thus requiring a different early postoperative DBS management. Accordingly, optimization of DBS in dystonia requires patience both on the treating and the treated side and may be time consuming for both parties. The present chapter summarizes available data on early postoperative management of dystonia following DBS and will supplement expert opinion not yet corroborated by peer-reviewed publications.

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Relevant conflicts of interest/financial disclosures: Nothing to report. Full financial disclosures and author roles may be found in the online version of this article.

Received: 24 April 2010; **Revised:** 30 November 2010; **Accepted:** 10 December 2010
Published online in Wiley Online Library (wileyonlinelibrary.com).
DOI: 10.1002/mds.23624

Materials and Methods

Search Strategy

The literature search was performed using PubMed, CINAHL, and the Cochrane Collaborative databases from 1980 to January 2008 using the terms *dystonia* AND *deep brain stimulation*, *pallidal stimulation* AND *dystonia*, *subthalamic stimulation* AND *dystonia*, *thalamic stimulation* AND dystonia, *secondary dystonia* AND *DBS*, and *neurodegenerative diseases* AND *DBS*. The search was combined with the one used for neuropsychology, neuropsychiatry, microelectrode recording, neuroimaging, electrophysiology, surgical techniques, complications, and targeting. Only English-language publications involving human subjects were considered. A total of 235 articles were retrieved. To facilitate the committee's work, the articles were divided into 3 overlapping groups: preoperative, intraoperative, and postoperative. A PDF file was created for each article obtained from the search and put on a CD that was mailed to members. During the writing phase, an additional 71 articles were added to update the search, covering the period from January 2008 to September 2009.

Process of Generating Clinical Recommendations

The committee members of the Task Force included neurologists, neurosurgeons, neurophysiologists, neuropsychiatrists, neuropsychologists, and nurses with expertise and experience in DBS for dystonia. The experts were also chosen from different countries (in Asia, Europe, North America, and South America) to provide a more comprehensive contribution to the Task Force. The authors of each chapter were selected, taking into account their specific expertise in the field. The steering committee prepared a list of questions related to the specific aspects of the 3 areas to be covered—preoperative, intraoperative, and postoperative—and established 2 chairs responsible for each of these 3 areas (subcommittees). These chairs then assigned a few questions to be addressed by each member of the subcommittees. The answers to the questions had to be formulated after reviewing the available literature and combining their expertise. Because the level of evidence for most of the DBS studies was low, the responses were organized according to the template previously used for the "Special Supplement on DBS for Parkinson's Disease (PD)": (1) available data, (2) conclusions, (3) pragmatic recommendations, and (4) points to be addressed.[1] A first document was prepared from this initial work and was reviewed and discussed by the entire Task Force group during a 2-day meeting. During the meeting the Task Force members provided further feedback and agreed on additional refinement of the whole document, adding the comments and remarks collected during the meeting. Special attention was given to formulating pragmatic recommendations in the absence of available studies. A second version of the project was sent to the entire working committee for final approval. The steering committee then met again to refine the "Special Supplement" document before submission.

Early Postoperative Period (0–4 Weeks)

Postoperative Recommendations

Do you consider postoperative imaging (MRI or CT scan)?

Available Data. Postoperative imaging is done in most of the centers that have published data on DBS and dystonia. This is critical to confirm the accuracy of lead placement, small intracranial bleeding, postsurgical edema, and documentation in the event of future possible lead displacement. Although some use CT scans or stereotactic CT scans, others use MRI scans. The available publications often do not state whether imaging is performed before implantation of the pacemaker[2] or afterward. Because there have been concerns about possible severe adverse events following MR imaging in patients with implanted electrodes,[3,4] recommendations for safe imaging settings have been given, limiting the specific absorption rate (SAR).[2,5] Accordingly, it appears that radiologists, who are not familiar with DBS, have become reluctant to perform brain MR scans in patients with implanted electrodes. Therefore, it has become an option to obtain postoperative CT scans that may be fused with preoperative MR scans to determine electrode position. Interestingly, a recent retrospective survey in main American DBS centers in more than 3300 DBS-treated patients revealed no permanent complications using a variety of MRI protocols except for 1 impulse generator (IPG) failure,[2] which complies with a single-center experience in more than 405 patients, not revealing any complications.[5] Thus, it is likely that SAR limitations will be revised in the future. Furthermore, it remains to be determined if future probabilistic, possibly automated approaches to calculating the position of the electrodes will help to improve the accuracy of the postoperative localization of the electrodes in the 3-dimensional space of the target structure.[6]

Conclusions. Imaging should be considered mandatory after electrode placement, specifically to exclude asymptomatic bleeding or gross misplacement of electrodes. The choice (CT or MRI) will depend on the specific prerequisites and available resources in the

individual DBS centers. A postoperative brain MRI (1.5 Tesla) seems to be safe if performed with certain precautions,[2,5] either prior to implantation of the IPG or after switching off the IPG prior to a postoperative MRI.[7] Conceivably, because of the increased contrast resolution of the basal ganglia, a structural MRI may allow more accurate assessment of the anatomical position of the electrode than would a CT.[6] Furthermore, MRI inversion recovery sequences have been shown to be an excellent tool for direct visualization of the GPi. These images can be fused to a stereotactic MRI or CT and may help to improve anatomical targeting of the GPi for the implantation of DBS electrodes.[8]

Pragmatic Recommendations. Postoperative imaging methods vary between centers. It has not yet been determined whether stereotactic CT scans or nonstereotactic MR scans are more advantageous. The choice of when the scans should be performed also differs. However, scanning the patient immediately after completion of the implantation has several advantages. Indeed, when the patient is still sedated, movement artefacts will be minimized. Imaging with the stereotactic ring allows for correction of the electrode position if necessary.

Points to Be Addressed. MRI safety and improved techniques for localization of electrode position (already mentioned) need further examination.

How long should antibiotics be given postoperatively?

Available Data. There are no available data on the requirements, dosage, and duration of antibiotic therapy in the early postoperative period. However, extensive clinical experience exists for other implantable devices such as cardiac pacemakers. Thus, most centers will agree to provide intravenous antibiotics from up to 1 day preoperatively until 2–3 days postoperatively—for instance, intravenous antibiotics every 8 hours as long as electrodes are externalized for test stimulation or neurophysiological recordings and continuation of that schedule for 2–3 days after the pacemakers have been implanted.

Conclusions. Antibiotics are given in the early postoperative phase, which complies with extensive general surgical experience (cardiac pacemakers), but there are no retrospective or controlled studies on this issue in DBS and dystonia.

Pragmatic Recommendations. It is considered mandatory that at least perioperative antibiotics should be administered, and it is recommended that postoperative antibiotic treatment be considered as long as electrodes are externalized. There is no consensus on which type of antibiotic should be used, but it seems reasonable that the regimen may be adopted according to general neurosurgical guidelines.[9]

Points to Be Addressed. There is some interest in studying whether there are different requirements of the antibiotic regimen for externalized versus internalized electrodes.

When is the ideal time to begin postoperative programming, and how long should the patient stay in the hospital after implantation?

Available Data. Compared with subthalamic or thalamic stimulation for PD, the microlesioning effect of pallidal electrode implantations in dystonia is less evident. However, a recent article found that in 8 of 9 dystonia patients who underwent bilateral GPi DBS, this effect was very pronounced in some of the patients and lasted up to 3 weeks.[10] In these 8 patients, the magnitude of the microlesioning effect predicted the degree of motor improvement 6 months after surgery. In contrast, the duration of the effect did not correlate with the clinical outcome.[10] The available literature, however, does not provide any evidence about the optimal time to start stimulation after surgery. From the randomized sham-controlled study of the German Dystonia Study Group,[11] it can be concluded that delaying the onset of stimulation for 3 months after surgery does not reduce the efficacy of pallidal DBS because the sham control group obtained the same level of benefit after switching to active stimulation. Nevertheless, from a practical point of view, there is no need to delay programming after surgery to observe therapeutic benefit during periods of test stimulation, although the progressive loss of this microlesioning effect during the programming might interfere with the choice of optimal setting.

There is no indication in the literature about the necessary duration of hospitalization after surgery. Many European centers keep patients hospitalized for 1–2 weeks after surgery to observe regular wound healing and to initiate programming, whereas other centers (predominantly in North America) discharge patients soon after implantation and perform wound control and programming on an outpatient basis. Comparative publications on this matter are missing (for Europe, see, for example, Meissner et al[12]). These different practices likely reflect local national reimbursement policies and may be less influenced by medical requirements.

Conclusions. Evidence-based recommendations are not available for either question. Postoperative programming may begin the day after connection of the electrodes with the IPGs. At this point, however,

microlesion effects may persist up to 3 weeks. Thus, postoperative programming may also be performed 1–3 months postoperatively, when the patient's conditions are similar to the baseline assessment.

Evidence-based recommendations concerning the duration of the hospital admission following implantation of the IPGs are not available. Most European centers will agree that at least a 3-day in-hospital stay after IPG implantation is recommended for wound healing and potential application of antibiotics. In addition, effective postoperative pain management during the 1–3 days following implantation of the IPG can require inpatient care. However, country-dependent reimbursement issues and personnel and bed availability may have to be taken into account.

Pragmatic Recommendations. When to start DBS programming to check benefits and side effects from stimulation settings varies in different centers from 2 days to 1 month or more postoperatively and likely reflects different reimbursement strategies in different countries. Regardless of the postoperative period of hospitalization, wound inspection and dressing and pain control in the first week after surgery should be provided to every patient.

Points to Be Addressed. Reimbursement issues, different health strategic plans, and facility availability dictate the various postoperative out- or inpatient strategies in North America versus Europe. Comparative studies aimed at outcome measures would be desirable but are not likely to be feasible in the near future because of differing health care traditions in the different countries.

How to proceed to find optimal stimulation contact—selection of optimal therapeutic contact (best benefit/adverse effect ratio, monopolar vs bipolar)

Available Data. The beneficial effect of pallidal DBS critically depends on the position of the electrode in the posteroventral region of the GPi,[13] which is thought to represent the sensorimotor territory of the nucleus. Within this relatively large volume, however, no specific *hot spots* for stimulation have been identified so far.[14] Because the pallidum is somatotopically organized, this concept (ie, lack of hot spots) may change with evolving techniques to better determine the localization of the electrodes.[6] Imaging studies may be useful to screen the most likely candidate contacts for chronic stimulation, but the choice of the contact should not rely only on anatomical information (eg, postoperative neuroimaging by CT or MRI) but also include functional tests. Because the beneficial effects of pallidal neurostimulation for dystonia may not be immediately obtained with acute stimulation, prolonged periods of continuous stimulation (hours or days) can be required to note any improvement on clinical examination.[15,16] However, phasic dystonic movements and patients with tardive dystonia can improve faster.[17–21] However, an acute stimulation challenge, in which a single cathode is tested in a monopolar mode at a fixed pulse width and frequency with increasing amplitude, is necessary to determine the threshold for acute stimulation-induced adverse effects, which would limit the therapeutic window. The most common reversible stimulation-dependent side effects are capsular effects (so-called tetanic muscular contractions), visual flashes (phosphenes,[22] ie, stimulation-dependent visual sensations, often described in the surgical scenario as "viewing stars"), dysarthria, dysesthesias, or worsening of dystonia (eg, Kupsch et al[11]), which depend on stimulation of the surrounding areas as reported by many groups.[8,11,23,24] In this context, capsular adverse events can be distinguished from worsening of dystonia by low-frequency DBS, which may cause rapid DBS-induced tetanic muscular contractions ceasing rapidly on termination of low-frequency DBS. Although real dysesthesias may be rare, contractions are common. However, dysesthesias may be the subjective experience of subthreshold contraction that may become obvious if voltage is increased. Although transient phosphenes can be accepted, muscle contractions or dysarthria should be avoided.

The information concerning the anatomical location of the contact coming from neuroimaging and/or intraoperative neurophysiology and, more importantly, the information about the therapeutic width of each contact from the challenging test are useful to determine which contact will be the first tested during chronic stimulation. Although most centers start with monopolar stimulation, others favor initial bipolar stimulation of 2 adjacent contacts.[18,21]

An algorithm to facilitate stimulation programming has also been proposed and used in a clinical trial conducted by the German Dystonia Study Group.[11] In this study, the acute effects of increasing amplitudes of high-frequency stimulation were tested for each electrode contact (a trial of at least 30 seconds) in monopolar mode (frequency, 130 Hz; pulse width, 120 μs) during the programming session. The contact for prolonged stimulation was selected on the basis of a reduction of dystonic hyperkinesia or the induction of phosphenes at a low threshold (suggesting proximity to the optic tract) or on the basis of neuroimaging studies (suggesting an electrode location at the ventral border of the pallidum in patients without acute stimulation effects).

Other centers[23] have proposed prolonged test periods of monopolar stimulation (eg, 24–48 hours up to weeks) through each contact of the electrode and clinical evaluation of the induced benefit to determine the optimal site of stimulation. The necessary duration of

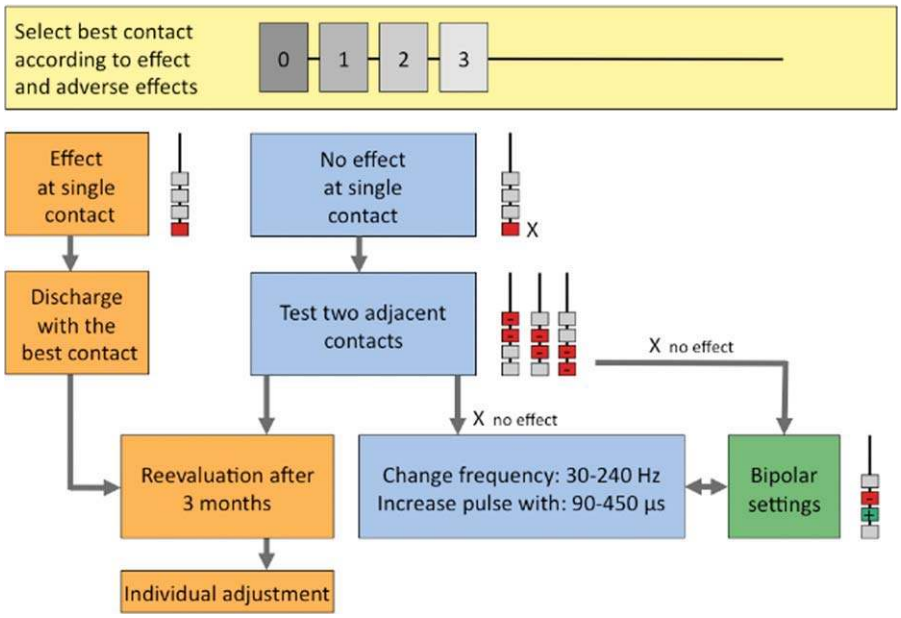

FIG. 1. Postoperative management algorithm. The algorithm depicts a proposal for the initial DBS programming in dystonia as used by the group in Berlin/Charité. In a first step, the effect/side effect ratio of the individual electrode contacts were determined. The patient was subsequently discharged with the "best" contact and might be reevaluated after a few weeks. During this, the amplitude of the contact might be increased to the highest tolerated intensity, that is, below the occurrence of side effects, if relief of symptoms was insufficient. If no effects on dystonic symptoms were observed at any contact, 2 adjacent contacts could be chosen systematically (monopolar stimulation) to increase the field of stimulation. If this approach did not allow for sufficient relief of symptoms, stimulation parameters might be varied as indicated, that is, a bipolar setting might be applied. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

stimulation to obtain unequivocal clinical benefit, however, is variable; possible synergistic effects of bilateral stimulation (especially on axial dystonia) could handicap clinical evaluation and lead to an unpractical long assessment period with multiple combinations to be tested.

Comparative studies assessing bipolar versus monopolar stimulation in the early postoperative management are not available. There are also no studies concerning the programming of bilateral stimulation starting with 1 side only and subsequent programming of the contralateral side after completing the first side.

There is no evidence that primary dystonias need a different programming approach than do secondary or other dystonias. However, different electrical parameters of stimulation might be needed (see below).

Conclusions. Evidence-based recommendations are not available due to lack of controlled studies. In contrast with STN DBS in PD patients with the potential occurrence of delayed dyskinesias, a so-called top-down or top-bottom approach (ie, using the highest voltage without the occurrence of adverse effects) may be used in dystonia, using bilateral monopolar stimulation for all 4 contacts, with symmetrical positioning of the bilateral electrodes provided, for 24 hours (rationale: delayed effects). The choice of the final electrode contact will depend on the best benefit/adverse effect ratios. Some centers[11] may also use phosphenes (ie, the contact above the induction of phosphenes, depending on the voltage[22]), if present, for the initial stimulation, but controlled studies to validate this pragmatic approach are not available, possibly also due to lack of phosphenes in a considerable number of DBS-treated patients with dystonia.

Pragmatic Recommendations. An algorithm for acute stimulation may be used (Fig. 1). This algorithm reflects the approach used by several German centers (for anecdotal evidence from 1 US center, see Ostrem and Starr[25]). With this approach, the first monopolar single-electrode contacts should be activated (Fig. 1, left) using a relative standard high frequency (130 Hz) and narrow pulse width (PW). Frequency and PW can be changed if satisfactory improvement is not achieved. Furthermore, 2 neighboring contacts may be activated (monopolar stimulation mode) to increase the stimulated field (Fig. 1, right). Bipolar stimulation with higher stimulation intensities may be also applied, aimed at focusing the stimulated field. In such a case, those electrode contacts that have been identified as located in the posteroventral lateral GPi by microelectrode recording or imaging will be used. Although a large stimulation field with all electrodes may be activated (not shown), this type of configuration might consume more energy and should be considered the last resource. In a last step, some large centers may use stimulation fields with all electrodes

activated (not shown), or frequencies or pulse widths may be modulated for the initial contacts used.

Points to Be Addressed. Future studies should address the issue of mono- versus bipolar stimulation in the initial programming session. Furthermore, the issue of starting the initial stimulation for primary and secondary dystonia needs to be addressed. In this regard, the French study group has chosen a similar approach in secondary dystonia.[26]

An interesting future approach could be the analysis of local field potentials at different electrode contacts within the GPi. Thus, pallidal local field potentials have been shown to be differentially affected in patients with dystonia versus patients with Parkinson's disease,[27] and pallidal local field potentials may be influenced by medication, for example, tetrabenazine, which may exacerbate beta activity in patients with tardive dystonia.[28] However, no controlled studies are available for assessing the usefulness of local field potentials to predict clinical optimization of electrode contacts in DBS-treated patients with dystonia.

How to proceed to find optimal stimulation settings (frequency, voltage, pulse width)

Available Data. A wide range of stimulation parameters has been shown to be effective for pallidal stimulation in dystonia. In particular, PW varies greatly between groups.[11,29–31] Different approaches have been reported accordingly (for a review, see reference 22). For instance, the Montpellier group has routinely employed a 450-μs PW.[32] However, few studies have systematically evaluated the impact of stimulation parameters on dystonic symptoms. Vercueil et al[33] did not find any significant difference in the severity of dystonic symptoms in primary generalized dystonia patients when the PW was varied between 60, 120, and 450 μs and the stimulation intensity adjusted to 10% below the threshold of adverse effects. This finding would also be expected from the theoretical chronaxy relation between pulse width and amplitude.[34] Because the current neurostimulation devices allow varying of amplitude on a much smaller scale than PW, it could be recommended that there be a relatively short PW (60–120 μs) and titration of the stimulation benefit by varying intensity, an approach that does not only reflect theoretical considerations but also points to energy costs/benefits, that is, an increase from 60 to 450 μs corresponds to an unproportionally higher increase in the battery current drain.

One study[35] evaluated the impact of stimulation frequency on dystonia severity in a double-blind, randomized study during short periods of acute stimulation (4 hours each) in patients with primary segmental and generalized dystonia. In this short-term observation period, they found a significantly better response to high-stimulation frequencies (130 Hz and above) compared with the placebo (0 Hz) and with lower frequencies (5 and 50 Hz). Recently, Alterman and colleagues,[23] based on their open-label observation, suggested that lower frequencies of stimulation (around 60 Hz) may result in a more favorable adverse effect/benefit ratio in certain subgroups of patients with primary generalized dystonia. These results still need to be confirmed. The benefits described in the available controlled clinical trials of pallidal neurostimulation for dystonia have been obtained with stimulation frequencies of 130 Hz or above,[11,30,36] and most groups are currently applying this stimulation pattern.

Moro and colleagues[24] investigated different stimulation parameters (pulse width, frequency, amplitude) in DBS-treated patients with cervical dystonia, showing that high frequency and high amplitudes predict a favorable outcome. This could suggest a differential profile of low-frequency DBS in primary focal versus primary generalized dystonia. However, no systematic studies are available assessing potential programming differences in patients with primary, secondary, focal, and generalized dystonia or dystonia with different genetic backgrounds.

Because the benefits of stimulation are often delayed in dystonia, it may be difficult to slowly titrate up the stimulation intensity depending on the clinical response. Therefore, some groups have proposed to initiate stimulation with an intensity adjusted (eg, 10%–15%) to below the threshold of inducing nonreversible adverse effects.[11] Once a stable clinical benefit is obtained, stimulation intensity could be gradually reduced until dystonic symptoms reemerge to avoid expendable high-stimulation intensities causing more rapid battery depletion. This approach has been applied in 1 controlled clinical trial[11] but has never been evaluated against alternative strategies.

It might be useful to investigate different parameters of stimulation in some secondary dystonias such as Huntington's disease,[37] neuroacanthocytosis,[38,39] and SCA,[40] but only larger studies can give more solid conclusions.

No data are available on the use of continuous versus cycling-mode stimulation.

Finally, alternative targets in the basal ganglia for the treatment of different types, including secondary dystonia, have been reported, but the as-yet anecdotal character of these reports would go beyond the scope of this review and does not allow for definite conclusions to be drawn concerning differential stimulation parameters in these alternative targets (eg, STN, VIM[37,41,42]) versus the established pallidal target.

Conclusions. Evidence-based recommendations are not available. Two multicenter studies[11,30] used 130 Hz, 90–120 μs, and amplitudes of 2–5 V for initial

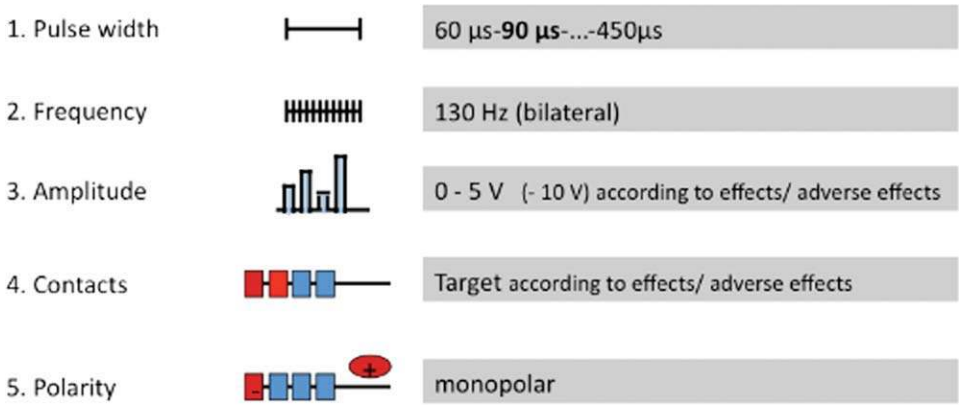

FIG. 2. Initial parameter setting of postoperative management algorithm. The initial stimulation parameters most used in pallidal DBS for dystonia are 130 Hz and 90 µs; amplitude was set below the threshold for occurrence of adverse events. Monopolar stimulation was used with the contact with the best effect/adverse event ratio. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

parameter settings in primary generalized and segmental dystonia patients. To note, the use of voltages above 3.6 V is not recommended for Soletra IPG (Medtronic, MN) because of the remarkable reduction of battery life. Because these parameters did not change substantially over a period of 3 years,[31] it is suggested to start with these settings. Usually most centers use 130 Hz to program GPi DBS-treated patients with primary generalized dystonia, although recent studies have found more benefit using 60-Hz stimulation.[23]

Pragmatic Recommendations. An algorithm for acute GPi stimulation for dystonia is provided in Figure 2. As indicated, primary bipolar stimulation is an alternative option.

Points to Be Addressed. Future studies need to address the issue of optimal frequency and disease-specific stimulation parameters (primary versus secondary dystonia).

What are the criteria to assess stimulation effects?

Available Data. GPi DBS mainly aims at improving motor disability induced by dystonia. There is no general consensus about which rating scales should be used in monitoring treatment effects. Most studies have used the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) to evaluate treatment effects in nonfocal dystonias.[11,30,31] The major downside of this scale is the lack of distinction between dystonic postures (fixed dystonia) and dystonic movements (mobile dystonia and dystonic tremor), which could be differentially affected by GPi stimulation. Studies on cervical dystonia have mostly used the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).[24] These dystonia scales have often been combined with ratings of daily function, quality of life, pain, and subjective well-being. In patients with myoclonus or dyskinesia-like movement disorders (tardive dystonia, Huntington's disease), more specific rating scales also should be used because of the above-mentioned restrictions of the BFMDRS (eg, Abnormal Involuntary Movement Scale, myoclonus scores).[18,43,44] Furthermore, psychiatric rating scales (eg, Beck Depression Inventory) have been used in patients with psychiatric comorbidities[18,43] and may help to unravel psychiatric complications pre- and post-DBS surgery. In this regard, it should be mentioned that dystonia scales are often insensitive to small changes. From a pragmatic point of view, it may be reasonable to focus on 1 prominent sign in a single patient. For instance, if the limbs are dystonic, one may choose stimulation parameters according to the response of this sign, including potential pain. Thus, global scales may be rather useful in assessing overall outcome. Fine-tuning using visual analog scales (VASs) may be preferable, but evidence-based III–IV studies are missing in this regard.

VASs may be helpful for the assessment of subjective sensations (pain, if not already scored in specialized scores such as the TWSTRS) and differing interpretations on the outcome of DBS surgery (patient, caregiver, medical personnel). Specific studies on outcome predictors such as pain or phasic and tonic movements or fixed postures are not available. Anecdotal reports and expert observations suggest that early relief of pain may positively correlate with postoperative improvement and suggest superior and faster improvement of phasic versus tonic versus fixed dystonia.

Myoclonus and tremor may improve early but have not been established as predictors of long-term improvement in DBS-treated patients with dystonia.

Furthermore, anecdotal reports suggest early (minutes to hours to days), target-dependent

improvement of myoclonus and tremor. In this regard, thalamic DBS seems to be associated with more rapid improvement compared with pallidal DBS.[45]

Conclusions. Evidence-based recommendations on the sensitivity and specificity of scales assessing postsurgical outcomes in DBS-treated patients with dystonia are not available. For acute and subacute evaluation in addition to disease-specific rating scales (cervical and generalized dystonia), VASs have been shown to be useful (see chapter on scales).

Pragmatic Recommendations. Validated scales for dystonia may be used to assess stimulation parameters in DBS-dystonia. Systematic comparative studies on their usefulness are not available. With respect to potential psychiatric side effects, the Beck Depression Inventory may be employed to monitor potential depressive symptoms. Furthermore, quality-of-life scales should be employed. Videotaping has been shown to be very useful to reassess dystonic states before and after DBS.[11,30,31]

Points to Be Addressed. Future studies should investigate the time course of DBS-induced symptom relief. Furthermore, scales that assess expectations before and after surgery may be useful for follow-up of DBS-induced effects but are not yet available. Quality-of-life scales may be useful however, they often lack disease specificity.

Troubleshooting in the Early Period

Adverse events related to stimulation and surgery (eg, skin infection, local hematoma)

Available Data. Data from 2 controlled studies on pallidal DBS in patients with generalized or segmental dystonia are available.[11,30] The French multicenter study reported 5 reversible adverse events (AEs) in 22 patients (44 electrodes), mostly stimulation-dependent or clinically asymptomatic AEs (including 1 intracerebral hemorrhage).[30] In the German multicenter study, a total of 22 AEs in 19 of 40 patients (total of 80 electrodes) were reported, all reversible, within an observation period of 6–9 months.[11]

Recently, a retrospective survey on serious adverse events (SAEs) during the first 30 postoperative days after DBS was performed in approximately 1200 patients with different movement disorders from 5 German stereotactic centers.[46] The mortality rate was 0.4% (causes of death were pneumonia, hepatopathy, and 1 case of complicated multiple sclerosis). The permanent surgical morbidity rate was 1%. The most frequently observed SAEs were intracranial hemorrhage (2.9%) and pneumonia (0.6%). Skin infection occurred in 5 of 1183 patients (0.4%). Surgical complications caused secondary AEs (eg, pneumonia) in elderly patients, who seem to be at higher risk for AEs, and in patients treated for PD.[47] Importantly, complication rates did not differ among the 5 centers. It remains to be determined if these data on patients with various DBS indications (predominantly PD) can be transferred to DBS in dystonia. Indeed, the complication rate is likely to be lower in DBS-dystonia because of the younger age of dystonia patients at the time of surgery. The mean age of DBS-treated dystonia patients is approximately 40–45 years, which contrasts with the mean age of approximately 60 years of DBS-treated PD patients.[48,49] Long-term hardware complications for DBS in PD amount to approximately 0.4% to 10.2% during different observation periods; whether this picture is transferable to DBS in dystonia remains to be determined. Furthermore, mood alterations including suicides have been reported in DBS-treated PD patients and anecdotally also in DBS-treated dystonia patients,[50,51] although classes I–III evidence-based data are missing for DBS-dystonia. Because mood alterations have not been reported in randomized, controlled trials in DBS-dystonia in contrast with PD patients treated with STN DBS, the incidence of this complication most likely is lower, and specifically the question of target dependence arises in this context.[46]

Conclusions. Permanent AEs in DBS dystonia are rare and were not observed in 2 controlled trials.[11,30] The absence of permanent AE in these 2 studies does not mean there are no SAEs in DBS for dystonia. In fact, it is likely that the general occurrence of AEs in DBS such as hematoma, pneumonia, and related mortality may be similar to that for DBS in ET or PD (for a review, see Hamani et al[52]). Infection of the stimulation system seems to be one of the most frequent SAEs, that is, requiring hospitalization of the patient. DBS-evoked adverse events are usually reversible on adjustment of stimulation parameters ($n = 2$ in the French study, $n = 4$ in the German study).

Pragmatic Recommendations. AEs related to DBS should be documented in a systematic way.

Points to Be Addressed. Future studies should address strategies to potentially lower perioperative infection risk. However, no controlled trials have been published so far. Furthermore, long-term hardware complications need to be assessed in DBS for dystonia.

How to combine stimulation and medication?

Available Data. No evidence-based data are available on handling medical treatment in DBS-treated patients with dystonia. However, antidystonia drugs could be distinctly reduced up to 50%–60% 5 years postsurgery (eg, Isaias et al[53]). Additional studies have reported

reduction of medical treatment at different points postsurgery[18,31,54,55] Very limited data are available on the interactions of stimulation and medication early after surgery by assessing the patient in both stimulation on and off states combined with medication on and off states.[56]

In contrast with STN DBS in PD, which usually requires reduction of medication to manage both levodopa- and stimulation-induced dyskinesia, the effects of pallidal DBS, in general, have not been reported to interfere with or counteract medical treatment. Thus, provided that medical treatment is tolerated and beneficial, there is no need to rapidly taper off medication.

Conclusions and Pragmatic Recommendations. In general, it is advised to keep the medical treatment unchanged for 1–3 months postoperatively (rationale: reduction of confounding factors for DBS programming). Then, medications may slowly be tapered off. In tardive dystonia, where DBS effects seem to be more rapid, tetrabenazine may be tapered off faster if drug-related AEs exist (such as parkinsonism, depression).

Points to Be Addressed. Future studies should investigate strategies for the management of medical treatment for dystonia after GPi DBS.

What is the specific knowledge necessary to do the programming?

Available Data. No evidence-based data are available on specific knowledge with regard to programming DBS-treated patients with dystonia.

Conclusions and Pragmatic Recommendations. The person who does the programming in dystonia patients should have expert knowledge of dystonia in general (type and distribution of dystonia) and of the devices as well as the neurophysiological principles of neurostimulation (voltage, pulse width, frequency, etc.). Anatomic knowledge should be thorough and comprise awareness of phosphenes and capsular effects during GPi stimulation. In addition, because in long-term follow-up new side effects might become evident, such as dysarthria, dysphagia, or akinesia,[37,57] particular attention should always be paid to unexpected effects while the programming is done.

Scheduling follow-up visits—what are the criteria for scheduling the next follow-up visits (3 months, 6 months, 1 year, then every 6 months or 1 year)?

Available Data. No evidence-based data are available on scheduling follow-up visits in DBS-treated patients with dystonia. In controlled trials and open observational studies, follow-up visits 3 and 6 months and subsequently 12 months postsurgery have been used.[11,30,31,53,58] This approach may miss clinical evidence of any improvement at an earlier time.

Conclusions. Because of the frequently delayed effects of DBS in dystonia, 1 follow-up visit after 1–3 months is reasonable. After the final programming (including all contacts; see Fig. 1), follow-up visits at 6-month intervals may suffice if stable relief of symptoms is achieved.

Pragmatic Recommendations. Routine follow-up at 4–12 weeks (see above: reimbursement issues) and subsequently every 6 months is recommended if no problems occur. Obviously, urgent or acute issues such as infections need to be promptly considered.

Points to be Addressed. None.

Should other targets or a new positioning in the same target be considered at this stage?

Available Data. There are no generally accepted guidelines for the management of therapeutic failure following initial stimulation. Reprogramming to alter electrode settings, altering PW and frequency may be considered, but resetting or adding additional electrodes should only be considered with longer follow-up (>6–12 months) to allow assessment of delayed DBS effects in dystonia. Thus far, few anecdotal studies have investigated the effects of combined or alternating thalamic versus pallidal stimulation[59–62] in different types of dystonia. In general, the therapeutic effect of thalamic DBS in addition to pallidal DBS appears to be limited,[59,62] but superior effects of thalamic stimulation have been reported in selected cases.[61]

Conclusions. Failure to improve at all in the first month of stimulation should be investigated.

Pragmatic Recommendations. It is mandatory to investigate therapeutic failures thoroughly. Accuracy of targeting, possible lead displacement, and/ or fractures should be excluded. Dysfunction of the electrodes or the pacemakers should be ruled out by routinely checking impedance and current flow. If there are side effects with stimulation, different stimulation settings should be explored. If failure to improve with either form of stimulation occurs, increasing PW and altering frequency can help. If misplacement of an electrode is detected, the position of the electrode should be corrected.

Points to Be Addressed. Consideration of alternative or additional electrodes should be evaluated after exhaustive testing, which normally takes 12 months; however, studies are lacking.

Treatment Until Stabilization (4 Weeks–6 Months)

Follow-Up Visits

Scheduling follow-up visit (3 months, 6 months, 1 year, then every 6 months or 1 year)

Available Data. Evidence-based data on the scheduling of follow-up visits to adjust stimulation parameters in DBS-treated dystonia patients are not available. However, numerous studies have investigated DBS-treated dystonia patients at different points, which may serve as a guideline for future studies and practical management. Thus, the following times have been reported.

The French Study routinely investigated patients 3, 6, and 12 months and 3 years postsurgery.[30,31] Patients were advised to return to the hospital when needed, that is, if they felt inadequate clinical benefit or experienced AEs. Only 6 patients attended the 1- and 3-year protocol visits. Two thirds of the additional visits (28 outpatient visits and 13 brief hospital stays) were related to the usual follow-up of medical treatment. Most visits were related to the control and adjustment of battery or stimulation settings. Three years postoperatively, the stimulation settings were similar to those reached after 1 year of follow-up.[31]

In the German multicenter study,[11] adjustments to stimulation settings were not allowed during the first 3 months of the study unless intolerable AEs occurred. However, adjustments were performed at any time thereafter to maximize the clinical benefit or reduce AEs. Evaluations were performed every 3–6 months thereafter.

Furthermore, the following information has been provided by other clinical case reports and case series. Whereas no information on times was provided by some study groups,[15,63,64] varying times and assessment protocols have been employed by French, German, and American study groups,[23,32,65–69] ranging from days to months. Anecdotally, stimulation parameters were changed on clinical grounds.[68] Because the effects of GPi DBS on dystonia may be delayed and gradual, it has been postulated that to be useful at least 24 hours of continuous stimulation on any 1 setting should be allowed before assessing the efficacy of stimulation.[69]

Conclusions. Generally, follow-up visits have not been standardized and seem to depend on the achievement of a satisfactory response or on the development of side effects.

Pragmatic Recommendations. There is no evidence favoring particular follow-up times after surgery. In general, too frequent adjustments should be discouraged, as clinical effects may occur several days or weeks after stimulation changes. If possible, systematic assessments 3, 6, and 12 months after surgery and then every 6 months to 1 year should be offered in order to address clinical outcome, device function, and battery life.

Points to Be Addressed. Studies are needed to establish the time when considering that a satisfactory response has not been achieved yet (ie, 6–12 months postsurgery).

Adaptation of parameter settings (propose a procedure, eg, increase voltage, then pulse width, modification of frequency [130 vs 60 Hz])

Available Data. (1) Programming procedure—because evidence-based data are missing, the following section lists available from the literature. Every group seems to have its own paradigm and routine, which are rarely explained in its rationale. Conceivably, Figure 1 tries to provide a pragmatic algorithm that summarizes the approach of several groups. Obviously, group-specific variants are justified by research-oriented or individual patient-oriented requirements.

—Programming guidelines for dystonia have been provided for instance by Kumar[69] and largely comply with the algorithm provided in Figure 1.

1. Determine *threshold for adverse effects* in a manner similar to that for PD.
2. Initially assess the efficacy of stimulation by using *high-stimulation frequency* (130–185 Hz) and *narrow PW* (60 μs, similar to PD) at an amplitude just below AE threshold by using *monopolar* stimulation for approximately 1 hour, with each electrode contact using monopolar stimulation. The best results are typically seen using the lowest (deepest) contacts.
3. If there is no acute benefit with stimulation, then more chronic stimulation *for 1–2 days* with the monopolar settings should be tested.
4. If no benefit is seen with narrow PW stimulation, it is then helpful to test the effects of *wider PWs (gradually up to 450 μs)*, with monopolar stimulation in a similar manner.
5. Depending on the results with the above test stimulation, it may also be useful to test the effects of *double monopolar* stimulation.
6. If no benefit is noted with short-term stimulation, it may be useful to employ the method described by the Montpellier group, that is, stimulation above the optic tract (usually with electrode 1) at 450 μs and 1–2 V (ie, just below the AEs threshold) and at high frequency.
7. Consider *low-frequency stimulation at 50 Hz*.[23]

For more detailed information on DBS dystonia programming, see references 11, 30, 63–65, 67, and 68.

(2) How to choose parameters—first-class evidence studies are missing.

Preliminary experience favors the use of more ventral electrodes in monopolar or bipolar stimulation mode, high voltage (except the Montpellier group), medium-high PW, and high-frequency stimulation.

Good empirical and documented evidence exists for active posteroventral contacts (0 and 1, using Medtronic software nomenclature). A cluster analysis of the stimulated contact coordinates was reported in 15 patients with primary generalized dystonia.[13] Two groups were identified who showed greater clinical improvement for posteroventral rather than anterodorsal stimulation for the arm and trunk. For the leg, posteroventral and anterodorsal stimulation achieved equivalent efficacy. Overall clinical improvement was maximal with posteroventral stimulation and inversely correlated with the *y* (A-P) coordinate.

The French study group investigated clinical effects of acute bilateral high-frequency ventral versus acute dorsal pallidal stimulation via the BFMDRS.[36] Bilateral acute ventral stimulation of the GPi significantly improved the BFMDRS score, by 42%, and resulted in chronic stimulation of contacts in the internal GP or medullary lamina in 18 of 21 patients. However, selection of parameters was not possible from the study design employed.

Voltage parameters have been empirically used below the motor or visual side event threshold (see above). Low motor thresholds for AEs may suggest misplacement of electrodes, either too ventrally or too anteriorly.[66]

Interestingly, short-duration stimulus PWs may be as effective as longer ones during a 10-hour period of observation.[33]

Empirically, high frequencies are employed by most studies, but selected studies suggest similar effects of low-frequency stimulation (LFS),[23] such as 50 Hz,[29,69] 50–60 Hz,[16] 25 Hz,[70] and 60 Hz.[23] In addition, LFS was successfully used in neuroacanthocytosis[39] and Huntington's chorea,[37] possibly suggesting differential effects of high versus low DBS in different dystonic disorders.

Conclusions. Evidence is based on retrospective analysis of individual strategies and not on systematic, prospective, and rational approaches. There is fairly good evidence that the use of rather ventral electrodes may be preferable (for leg dystonia, also more dorsal) in monopolar (or bipolar) configuration, with voltage set just below motor (or visual) AE threshold. Very wide and narrow PWs have been found to be effective, as well as higher (130–185 Hz) and lower (50–60 Hz) stimulation frequencies.

Pragmatic Recommendations. A systematic approach to optimizing the stimulation parameters is recommended. Ventral contacts (if close to the optic tract, as evidenced by imaging or induction of phosphenes) with monopolar or bipolar configuration should have an early priority (although not exclusive) at the submaximal tolerated voltage. Narrower PWs (60–210 μs) and a 130-Hz frequency have been used more commonly and should be employed first. However, lower frequencies (60 Hz) may also be considered.[23] Wider PWs and higher frequencies can be as effective and may be taken into account as well.

Points to Be Addressed. Present published reports have exclusively applied continuous stimulation, and to date this parameter setting is recommended. Cycling stimulation (eg, 30 seconds off or day/night cycle) is under study without published reports yet.

Assessment of beneficial and adverse effects of stimulation

Available Data. No specific scales have been developed to assess clinical effects of chronic stimulation. To evaluate the impact of chronic stimulation, the BFMDRS[11,13,15,23,30,54,63,65,67,68,71–73] and the UDRS[67,74] for generalized dystonia, the TWSTRS,[16,21,55,67,71,75] and the Tsui scale[63] for cervical dystonia have been employed. In addition, several other scales have been used to assess other variables. For quality-of-life assessment (for a review, see Diamond and Jankovic),[76] the SF-36[11,30,63,75,77] and the PDQ-39[54] have been used. For neuropsychological and affective outcomes, there have been different instruments used: the Mini–Mental State Examination and the Mattis Dementia Scale, as well as Beck's Depression Inventory.[11,30,54,78] The Brief Psychiatric Rating Scale and the Beck Anxiety Inventory have also been used.[78]

Conclusions. Whereas no rating scales have been developed specifically for DBS in dystonia, validated rating scales have been variably used. Most studies employed the BFMDRS (for generalized dystonia) and the TWSTRS (for cervical dystonia). Quality-of-life studies have mainly employed the SF-36, whereas neuropsychological studies have employed a variety of batteries, which showed improvement of depression and stable cognitive performance in most instances. There is no evidence in the literature of systematic tools for assessing side effects.

Pragmatic Recommendations. It is necessary to systematically address benefits and side effects in DBS patients using available rating scales. The BFMDRS (for generalized dystonia), the TWSTRS (for cervical dystonia, and the SF-36 have been widely used and

allow ready comparison with previous literature. Systematic evaluation of side effects, possibly using standardized screens, is also recommended. A benefit/adverse effect battery should been checked as the patient is followed up at least once a year.

Points to Be Addressed. Further studies should address the relevance of motor and nonmotor outcomes by using appropriate scales after surgery in dystonia patients with DBS.

Control of parameter settings at each visit: pulse width, frequency, voltage, current flow, impedance, or only a few of them?

Available Data. There are no data available about the need to document or control the parameter settings at any visit, especially if patients are clinically stable.

Conclusions. There are no formal studies assessing control of settings needed at each visit.

Pragmatic Recommendations. It is important to check all the stimulation parameters (and document them on medical records) at every follow-up visit, especially if they are not frequent. In particular, impedance and current drain should be recorded in order to monitor device function and battery life. These operations take only a few additional minutes with commercially available technology. It is suggested that the patient have a copy of the records.

Evaluation

Should standardized evaluation be performed preoperatively and postoperatively (6 months, 1 year, or both) and how? When should the patient have developed the best possible response (optimal comparison with the preoperative condition)?

Available Data. Most available studies concerning primary generalized, cervical or other focal dystonias[11,13,15,16,19–21,23,30–32,54,55,63,64,66,68,70–72,74,75,79–91] and other studies concerning heterogeneous groups of secondary dystonias[17,43,59,65,80,83,85,86,92–102] have used validated scales to assess the efficacy of pallidal stimulation (BFMDS, TWHSDS, UDRS, etc.) before and after surgery. For tardive dystonia, which may involve dystonia, chorea, myoclonus, and tremor, more composite scales may be appropriate such as the Abnormal Involuntary Movement Scale or the Extrapyramidal Symptoms Rating Scale.[17,43]

The interval between surgery and the postoperative evaluations comprises between 3 and 12 months[11,13,15–17,19–21,23,30–32,43,54,59,63–66,68,70–72,80,82–91,94–102] All these studies have clearly shown that improvement usually starts within the first hours or days after the beginning of stimulation, with subsequent further improvement over weeks or months. Most of the benefit is usually obtained after 3 to 6 months.[11,13,15–17,19–21,23,30–32,43,54,59,63–66,68,70–72,80,82–91,94–96,102] Some additional improvement can occur later but, usually, to a less extent and more slowly. In some studies, however, an additional 30% improvement of the dystonia has been shown between 1 and 1.5 years later.[21]

Conclusions. Validated scales are widely used that appear reliable for drawing conclusions about the efficacy of DBS in dystonia. Controlled (blinded) studies are rarely performed but certainly provide the most valuable information regarding the efficacy of DBS in dystonia. After surgery most of the benefit is usually obtained after 3–6 months. Thus, regular follow-up visits are recommended every 3–6 months early postoperatively and every 6–12 months after 1 year postoperatively.

Pragmatic Recommendations. The use of standardized scales and videotaping is important in order to keep a precise picture of the disease before and after DBS surgery. Therefore, a video protocol should be used widely. The use of validated scales is warranted. In addition, it seems reasonable to determine the benefit 6 months after surgery but to keep evaluations, for example, every year.

Points to Be Addressed. The best time frame to assess the efficacy of DBS in each form of dystonia needs to be determined, as well as whether there are differences between primary generalized, cervical, and secondary dystonia. The issue regarding which scales are the most appropriate for assessing outcomes in specific types of dystonia also needs further investigation.

Should evaluation in the OFF stimulation condition be performed routinely or as part of research protocol? How long and when should OFF stimulation be maintained?

Available Data. Evaluations have been performed only anecdotally in the off stimulation condition.[11,16,18,30,31,43,70,82,90,95] However, these assessments can provide important information about the immediate effect of the stimulation and the delay of reoccurrence of the clinical signs, not only the long-term efficacy of the treatment. These studies may also allow a comparison with the preoperative motor situation and give an idea if disease progression is present. The duration of the off stimulation period before doing the assessment is variable. This question has been specifically studied by Grips et al,[90] who showed that most of the phasic motor symptoms reoccur within 4 hours, whereas the tonic signs may take

longer to worsen. In the French study group, the maximum tolerated duration of the off period was 7 hours. In a single case study of Lesch-Nyhan syndrome, the stimulator could be switched off for 1 month.[95] Goto and Yamada[16] described a patient in whom dystonic features did not worsen for months after bilateral GPi stimulation was discontinued following replacement of the IPG. These reports suggest that the posteffect of the stimulation may partly depend on the etiology of the dystonia. Tardive dystonia may worsen very quickly after stimulation has been switched off.[18,43] Furthermore, it is necessary to take into account the risk of major worsening of dystonia that may be life-threatening and has to be prevented by careful follow-up of the patient during this period. In the French Spidy study (2005), stimulation had been turned off 10 hours before the assessment, but no patient could tolerate more than 7 hours of off duration. Furthermore, bilateral[24] GPi stimulation was blindly turned off in 8 patients with cervical dystonia. Two patients dramatically worsened within 1 hour, whereas the median to reach the preoperative motor score was 2.8 hours (range, 0.25–24 hours).

Conclusions. The off stimulation condition evaluations have only been performed so far in a few studies and for research purposes. Although this condition creates obvious discomfort for patients, off stimulation assessments provide interesting data concerning the posteffect duration of DBS in dystonia. Turning off the stimulator for a defined period in patients with established benefit should be done under controlled situations, with the patient informed about the procedure. If the patients have a patient review device (Access), they should be trained to use it properly.

Pragmatic Recommendations. A reasonable duration of the off period of around 3 to 4 hours might be satisfactory, even though this may not lead to the worst-off condition. Routinely, the off stimulation evaluation does not appear useful with respect to the risk of clinical deterioration and associated ethical constraints.

Points to Be Addressed. The delay in motor signs reoccurroing as a function of the etiology of the dystonia should be investigated.

Adaptation of medications—use of botulinum toxin (pain, local contracture, laryngeal dystonia, residual focal dystonia, eg, neck)?

Available Data. The majority of the studies report that antidystonic medications could be reduced or even tapered off completely after surgery.[11,13,15–17,19–21,23,30–32,43,54,59,63–66,68,70–72,80,82–91,94–96,98,100,101] However, the percentage of reduction has been variable and often not described in detail. In a study on primary generalized dystonia, half the patients stopped their drugs, whereas the other half reduced it by 50%.[23] In another study on cervical and generalized dystonias, one third of the patients could stop their drugs, and 1 patient continued to receive botulinum toxin after surgery.[71] Halbig et al[54] showed that two thirds of their patients (generalized dystonia) reduced or abandoned their treatment. Similar results were obtained in cervical dystonia.[55] Kupsch et al[11] demonstrated that among 20 patients with primary generalized dystonia, drugs could be reduced by 32% after 6 months and that 5 patients stopped all medication. In tardive dystonia, it was interesting to note that antipsychotic drugs did not have to be increased after surgery, which indicates that they are well tolerated in carefully selected patients also from a psychiatric point of view.[18,43] There is practically no information available on the use of medication and additional botulinum toxin injections in prolonged follow-up.

Conclusions. Bilateral pallidal DBS leads to a reduction of antidystonic medication as well as the use of botulinum toxin. However, it has to be noted also that dystonia patients scheduled for DBS are often only mildly improved by drugs. Slow reduction of medications over weeks or months is recommended as tolerated to reduce related AEs.

Pragmatic Recommendations. In clinical practice, antidystonic drugs can usually be reduced or even stopped without major problems. Drugs related to mood disorders or anxiety should be considered separately and should be changed in close psychiatric cooperation (slow withdrawal or reduction).

Points to Be Addressed. Evidence-based data are sparse. If incomplete relief of symptoms persists despite optimized stimulation protocols, additional Btx application may be considered as established for the treatment of focal dystonic or spastic symptoms, for example, local pain or laryngeal dystonia.

Specific Considerations for Secondary Dystonias

How do we determine the objectives (patient's and physician's objectives)?

Available Data. Ideally, the objective would be the disappearance of dystonia and disability related to dystonia with DBS surgery, without any stimulation-induced side effects and other complications. Although this aim can be partially achieved in primary dystonia, the existing literature shows much less favorable results in secondary dystonia, with the potential exception for some patients with tardive dystonia.[18,26] DBS is clearly less effective in generalized dystonia secondary to birth injury, suggesting that widespread

dysfunction of the sensorimotor pathways may be present and cannot be restored to a more physiological pattern by pallidal DBS.[26] In this context, it is important that not only physicians but also patients and their caregivers (especially of children) have realistic expectations. Despite the relatively mild improvement that can be assessed using standard motor scores, patients' self-assessments have been satisfactory in several instances.[20] In particular, the treatment of secondary spinal problems also has to be considered.[103]

Features that should not be expected to improve include fixed deformities and arthrosis secondary to dystonia, pain and disability related to secondary arthrosis, neurologic symptoms related to secondary myelopathy, nondystonic neurologic symptoms (eg, spasticity, cognitive dysfunction), and nonneurologic symptoms that are part of the syndrome. Speech and swallowing problems, even when related to dystonia, most often are not improved and occasionally may worsen with pallidal DBS.

Mobile aspects of a dystonic syndrome (tremor, chorea, choreodystonia, and myoclonus) are often more likely to improve than tonic or fixed aspects of dystonia. Slow movements in the context of widespread cerebral damage (eg, postanoxic dystonia), such as slow individual finger movements (athetosis) and slow, slurred speech, are generally not improved. The efficacy of DBS may evolve (generally in a progressive way) during the stabilization period (4 weeks–6 months). On the one hand, the patient should be aware of the potential progressive nature of improvement. However, if there is no or only little improvement after 6 months of chronic DBS, then the patient's expectations may need to be adjusted. In this context, avoiding further deterioration of secondary complications may be part of the objectives of DBS in dystonia.

Conclusions and Pragmatic Recommendations. Secondary dystonias benefit from pallidal DBS to a lesser degree than do primary dystonia.[26] However, with respect to limited therapeutic options in these disease entities, trials of reversible therapeutic interventions such as DBS will be performed in these patients but should be preferably performed within defined study conditions. In this context, the above-listed recommendations for primary dystonia apply.

Points to Be Addressed. A better definition of differential therapeutic responses in primary versus secondary dystonia following DBS is needed. Identification of predictors for DBS responders in secondary dystonia should be investigated. Patients' self-assessments of outcome should also be considered under these circumstances.

How to evaluate the possible discrepancy between "objective results" (eg, quantification by scales) and the patient's opinion (patient may be satisfied despite improvement appearing to be mild or moderate)

Available Data. No evidence-based data are available on this issue. In case the patient has an obvious placebo effect, the objectives could be met for that patient but not for the physician. In this case, there is no need to convince the patient that the outcome is not up to expectations. Especially those patients who have grown up with a disability often have good acceptance of and good functional adaptation to their disabilities.

In other patients the objective improvement may be minimal, but the same patients might rate their benefit as gratifying because they have better function in some activities, even though their motor function is far from normal. In these cases, it is recommended that separate VASs be employed for patients, caregivers, and doctors. It is noteworthy that the placebo effect in patients with dystonia treated with DBS seems to be quite low in randomized studies (less than 5%[11]), contrasting, for instance, neurosurgical transplantation studies in PD[104,105] with a placebo effect of up to 30%.

Acknowledgments: We thank Dr. Patricia Limousin for critical comments on earlier versions of the manuscript and Dr. Anatol Kivi for providing Figure 1.

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